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Case Report

Nocardiosis 'great imitator': unusual disease with usual presentations at unusual site

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ABSTRACT

Nocardia, an aerobic actinomycete, typically affects immunosuppressed individuals, commonly manifesting in the lungs. Cutaneous infections, particularly by *N. pseudobrasiliensis*, can occur, presenting as lympho-cutaneous, superficial, or mycetoma subtypes. *Nocardia farcinica*, resistant to third-generation cephalosporins, is particularly virulent. A 50-year-old female with type 2 diabetes presented with painful nodules, bullae, and recurrent discharge over the left wrist, mimicking cellulitis. Culture-sensitivity revealed *Nocardia farcinica*. Treatment involved debridement, De quervain release and prolonged Linezolid therapy for a complete cure. Cutaneous Nocardiosis can mimic cellulitis, posing diagnostic challenges due to slow growth and microbiological detection. *N. farcinica* demonstrated resistance to conventional antibiotics. This case emphasizes the importance of considering Nocardia infections in diverse clinical presentations, highlighting the need for a comprehensive diagnostic approach, especially in immunocompromised individuals.

Keywords: Antibiotic therapy, Cutaneous nocardiosis, Dequervain tenosynovitis, Immunocompetent hosts, *Nocardia farcinica*

INTRODUCTION

Nocardia is an aerobic pathogen belonging to genus actinomycetes that lives in water and soil. It is rod-shaped, filamentous and gram positive bacteria which commonly affects lungs in patients with immunosuppressed status like those of cancer, AIDS and organ transplantation.[1] Those infected with nocardia remain asymptomatic for a long duration of time as the bacteria is slow to grow and thus cannot be isolated in specimens.

Cutaneous infections (most commonly by N. pseudobrasiliensis) are usually seen on feet in immunocompetent hosts and are of three subtypes namely (1) lympho-cutaneous (clinically similar to sporotrichosis), (2) superficial, and (3) mycetoma (chronic infection with discharging sinuses).[2]

CNS spread though less common can be fatal as seen with systemic involvement in immunocompromised patients.[3] Centres for disease control and prevention reckons around 500-1000 cases annually in US. Nocardia takes around two weeks to 1 month to grow in culture media and also as cutaneous and pulmonary infections often being polymicrobial in origin in addition to less application of molecular diagnostics further attenuate the chances of its isolation.[4] In a patient infected with nocardia, treatment with empirical antibiotics decrease the symptoms but renders ineffective in complete cure of the disease.

Catalase and superoxide dismutase (SOD) produced by nocardia inhibit phagosome-lysosome fusion, lower intracellular acid phosphatase levels ,secrete toxins and evade the host immune response are all factors that contribute to its virulence.[5] In addition, it is known that

Nocardia L-phase/cell wall deficient variants, can be produced within the lungs and have a role in pathogenesis in animal models. However, these forms are not recovered from infected lungs, which makes identification challenging and has been linked to the disease's latency.[6] Adding to difficulties with diagnosis and eluding immune resistance, strain identification has an impact on how well a treatment works. With genome sizes between 6 to 10 million base pairs (Mbp), Nocardia species exhibit significant heterogeneity.[7] The virulence and susceptibilities to antimicrobials of different pathogenic Nocardia species are very different from one another. The clinically important Nocardia species are divided into 13 antibiotic susceptibility patterns.[8] Third-generation cephalosporins are among the drugs that *Nocardia farcinica* is naturally resistant to, making it most virulent of the nocardia family. Main pathogenic species include *N. nova*, *N. pseudobrasiliensis*, and *N. cyriacigeorgica* as well. The species vary from one another in terms of biochemical traits including their capacity to use various carbon sources and hydrolyse various substrates.[9]

These variances are all taken taken into account when delineating a species. Such methods, nevertheless, are time-consuming and call for a high degree of expertise. Owing to this, many clinical laboratories seldom distinguish between different species of Nocardia infections.[10]

Given the possibility of relapse, nocardiosis treatment is frequently prolonged once it has been identified.[11] Antibiotic therapy for immunocompetent patients must last for six to twelve months, and for immunosuppressed individuals or those with CNS dissemination, treatment must last at least twelve months. Regardless of the different susceptibility patterns across the Nocardia species, all 13 patterns exhibit sensitivity to linezolid and the trimethoprim-sulfamethoxazole combination medication.[12] Third-generation cephalosporins and aminoglycosides like amikacin are also employed, and combination therapy can improve outcomes.[13]

CASE REPORT

A 50 years/female with type 2 diabetes on treatment presented to the out-patient department with complaints of severe pain and nodules over the dorso-radial aspect of left wrist and thenar eminence since 7 months not responding to treatment by NSAIDs. She complained about pustules, nodules and bullae formation (Figure 1) with purulent and serosanguinous discharge (Figure 2) which recurred in a waxing and waning pattern.

She did not recall any trauma or insect bite. On clinical examination, she was afebrile, vitally stable and no enlarged lymph nodes found. Local examination ascertained presence of redness, tense tender swelling (Figure 3) with serosanguinous discharge from bullae mimicking cellulitis and tenderness overlying dorsoradial aspect of wrist. Finkelstein and Eichhoff's test were positive suggestive of 1st compartment stenosing tenosynovitis. Routine investigations suggested raised leukocyte count with controlled blood sugars and ruled out anything challenging her immunocompetence. Local ultrasound suggested

Dequervains tenosynovitis with subcutaneous edema and fluid collection in volar aspect of wrist. Conservative management with empirical antibiotics mildly reduced the pain and swelling but recurred with draining sinuses (Figure 4) on stopping the treatment. Pus and necrotic tissue was debrided after dequervain's release and sent for culture and histopathology evaluation. Culture-sensitivity report isolated *Nocardia farcinica* from Nocardia species sensitive to both linezolid and trimethoprim-sulfamethoxazole. Patient was started on Linezolid mono-therapy.

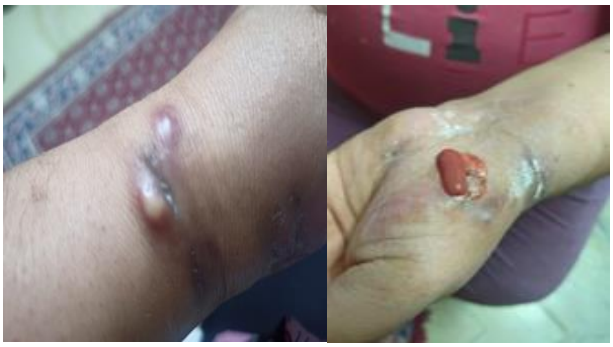

Figure 1: Nodules and bullae over volar aspect of left wrist.

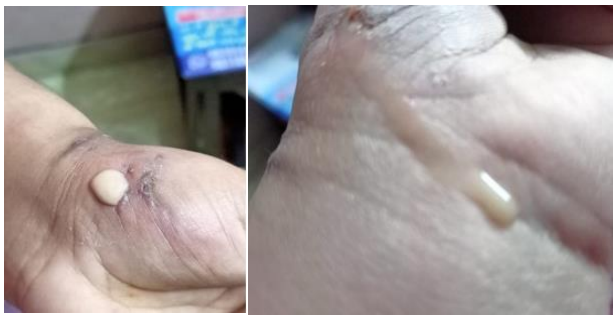

Figure 2: Volar aspect of left wrist showing nodule with purulent discharge.

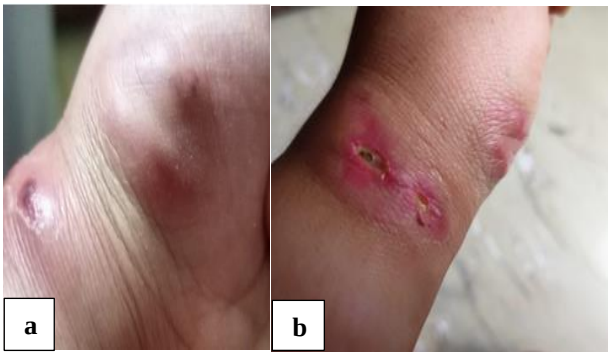

Figure 3: (a) Tense swelling; and (b) draining sinuses.

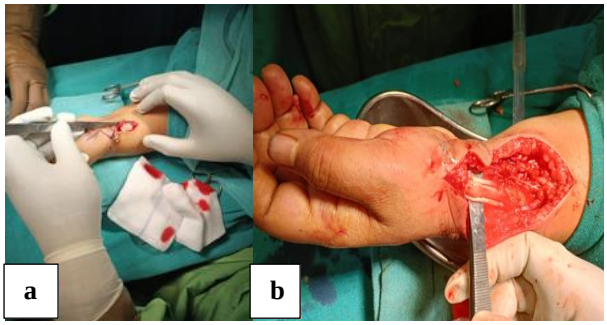

Figure 4: (a) Pus pocket; and (b) post debridement and DC1 release.

DISCUSSION

The identification and treatment of Nocardia infections pose significant challenges due to the diverse nature of the pathogen and its varying susceptibility patterns across species. Our findings align with previous studies concerning the slow growth of Nocardia species, making their microbiological detection cumbersome.[1,4] Virulence factors produced by Nocardia, such as catalase, superoxide dismutase (SOD), and L-phase/cell wall-deficient variants, contribute to its evasion of the host immune response. This delayed identification underscores the importance of considering Nocardia as a differential diagnosis in cases where clinical manifestations mimic those of other more commonly encountered bacterial or fungal skin infections.[2,10]

Our case presentation, focusing on a 50-year-old female with type 2 diabetes presenting with cutaneous nodules, bullae formation, and serosanguinous discharge, highlights the complexities in diagnosing primary cutaneous nocardiosis.[2,5] This case was clinically indistinguishable from other skin infections, resulting in delayed identification despite routine investigations.[2,10] Surgical intervention became necessary due to the persistence of symptoms despite conservative management. Careful dissection preserving the superficial branch of the radial nerve revealed a pus pocket during the procedure. Debridement with drainage and DC1 pulley release was performed under general anaesthesia, aiding in the management of the infection.

In accordance with previous reports, our patient's infection involved the upper extremities, a less common occurrence.[2,3] Furthermore, the persistence and relapse of infection in the presence of diabetes might suggest a role of host factors influencing the disease's course, as observed in similar cases.[11,13]

Microbiological identification of *Nocardia farcinica* from the culture-sensitivity report highlighted the importance of antimicrobial susceptibility testing.[4,8] This aligns with previous studies emphasizing the need for susceptibility testing due to varied susceptibilities of Nocardia species to antimicrobials.[8,12] The choice of linezolid as a mono-therapy, in our case, echoes successful outcomes documented in other reports and guidelines.[8,12]

While our case mirrors several attributes described in literature regarding the clinical presentation and treatment of cutaneous nocardiosis, the challenges in identifying and treating these infections persist. Comprehensive studies comparing the efficacy of various treatment regimens and their outcomes in diverse patient populations are warranted.[1,5,7,9]

CONCLUSION

Primary cutaneous nocardiosis affects immunocompetent hosts and the most common subtype producing cutaneous illness, as in our case, is *N. Nocardia farcinica* which is most virulent owing the resistance to conventional antibiotics. Although the actual prevalence of soft-tissue nocardiosis appears to be modest and much less in upper extremities, many cases may go misdiagnosed due to challenges in microbiological diagnosis. Our example implies that primary cutaneous nocardiosis should be included in the diagnostic route in cases of cellulitis especially in that involving hand and wrists.

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